image.

PTO/SB/21 (08-00)

| | | Application Number | k Office: U.S. DEPARTMENT OF COMMERCI mation unless it displays a valid OMB control numbe 09/715,983 |
|---|----------------|---|--|
| TRANSMITTAL | | Filing Date | November 20, 2000 |
| FORM | | First Named Inventor | Brett P. Monia et al. |
| | nitial filing) | Group Art Unit | 1635 |
| to be used for all correspondence after i | iitiai iiiiig) | Examiner Name | J. Zara |
| tal Number of Pages in This Submission | | Attorney Docket Number | ISIS0057-100 (ISPH-0519) |
| tal Number of Pages III This Submission | | OSURES (check all that apply) | 1010000. 100 (1011) |
| Fee Transmittal Form | Assign | ment Papers Application) | After Allowance Communication to Group |
| Fee Attached | Drawin | | Appeal Communication to Board of Appeals and Interferences |
| Amendment / Response | Licens | sing-related Papers | Appeal Communication to Group (Appeal Notice, Brief, Reply Brief) |
| After Final | Petitio | n | Proprietary Information |
| Affidavits/declaration(s) | | n to Convert to a sional Application | Status Letter |
| Extension of Time Request | Power and C | r of Attorney with Revocation change of Correspondence | Other Enclosure(s) (please identify below): |
| Express Abandonment Request Information Disclosure Statement | Termi | nal Disclaimer est for Refund lumber of CD(s) | 1) Table A 2) Statement Under 37 CFR 3.73(b) with executed Assignment 3) Return Postcard |
| Certified Copy of Priority Document(s) | Rem | arks | |
| Response to Missing Parts/ Incomplete Application | | | |
| Response to Missing Parts under 37 CFR 1.52 or 1.53 | | | |
| SIGN | ATURE OF | APPLICANT, ATTORNEY, | OR AGENT |
| Firm or Paul K. Legaard, Individual name | Registration | No. 38,534 | |
| Signature Pert | y f | <i>e</i> | |
| Date September 26, 2 | 003 | | |
| | | ERTIFICATE OF MAILING | |
| I hereby certify that this correspondence addressed to: Commissioner for Patent | | | stal Service as first class mail in an envelophis date: September 26, 2003 |

Burden Hour Statement: This form is estimated to take 0.2 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be send to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

Signature

September 26, 2003

Date



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Assistant Commissioner for Patents Washington, DC 20231

Sir:

POWER OF ATTORNEY WITH REVOCATION AND CHANGE OF CORRESPONDENCE ADDRESS

| I hereby revoke all previous powers of attorney or authorizations of agent given in the patents/applications identified in Table A attached hereto, and appoint PLATERIAL BAR COOK 413 SERE PATENT TRADEMARK OFFICE |
|---|
| as rny/our attorney(s) or agent(s) to prosecute the patents/applications identified in Table A, |
| and to transact all business in the United States Patent and Trademark Office connected therewith. |
| Please change the Correspondence Address for the patent applications identified in Table A to: Practitioners at Customer Number: 34138 |
| I am the: Applicant/Inventor. Assignee of record of the entire interest. (A statement under 37 CFR 3.73(b) is enclosed.) |
| Respectfully submitted, ISIS PHARMACEUTICALS, INC. |
| |

By:

::ODMA/PCDOCS/PHILA1/1821739/L

Name: B. Lynne Parshall Title: Executive Vice President



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Assistant Commissioner for Patents Washington, DC 20231

Sir:

STATEMENT UNDER 37 CFR 3.73(b)

Applicant, ISIS Pharmaceuticals, Inc., a corporation, states that it is:

the assignee of the entire right, title, and interest of the patents/applications identified in Table A attached hereto.

The extent (by, percentage) of its ownership interest is 100% in the patents/applications identified in Table A.

By:

X a copy of the pertinent assignment from the inventor(s) of the patent applications identified in Table A is enclosed herewith.

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

Respectfully submitted,

ISIS PHARMACEUTICALS, INC.

Date: 7/22/2003

Name: B. Lynne Parshall

Title: Executive Vice President

DOCKET NO.: ISPH-0519 PATENT

ASSIGNMENT

WHEREAS, We, Brett P. Monia, of La Costa, State of California; Lex M. Cowsert, of Carlsbad, State of California, Susan Murray, of Poway, State of California, Madeline M. Butler, of Rancho Santa Fe, State of California; and Nicholas M. Dean, of Olivenhain, State of California, have invented a certain invention entitled Antisense Modulation of P13K P85 Expression, for which we have made application for Letters Patent of the United States, said application having been filed November 20, 2000 and assigned Application No. 09/715,983; and

WHEREAS, ISIS Pharmaceuticals, Inc. hereinafter referred to as the assignee, of 2292 Faraday Avenue, Carlsbad CA, a corporation of Delaware, is desirous of acquiring the entire right, title and interest in and to the said inventions or improvements and in and to the said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in any and all countries:

NOW, THEREFORE, for and in consideration of the sum of One Dollar (\$1.00) to each of us in hand paid by said assignee, and other good and valuable consideration, the receipt of which is hereby acknowledged, we, the said assignors, have sold, assigned, transferred and set over, and by these presents do hereby sell, assign, transfer and set over to said assignee, the entire right, title and interest in and to said inventions or improvements and said application and any and all continuations, divisions and renewals of and substitutes for said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in the United States and any and all other countries, and any reissue or reissues or extension or extensions of said Letters Patent, and assign to and authorize said assignee, to file in our names applications for Letters Patent in all

DOCKET NO.: ISPH-0519 PATENT

countries, the same to be held and enjoyed by said assignee, its successors, assigns, nominees or legal representatives, to the full end of the term or terms for which said Letters Patent respectively may be granted, reissued or extended, as fully and entirely as the same would have been held and enjoyed by us had this assignment, sale and transfer not been made.

AND we hereby covenant that we have full right to convey the entire interest herein assigned, and that we have not executed and will not execute any agreement in conflict herewith, and we further covenant and agree that we will each time request is made and without undue delay, execute and deliver all such papers as may be necessary or desirable to perfect the title to said inventions or improvements, said application and said Letters Patent to said nominees, successors, assigns, its assignee, representatives, and each of us agrees to communicate to said assignee or to its nominee all known facts respecting said inventions or improvements, said application and said Letters Patent, to testify in any legal proceedings, to sign all lawful papers to execute all disclaimers and divisional, continuing, reissue and foreign applications, to make all rightful oaths, and generally to do everything possible to aid said assignee, its successors, assigns, nominees and legal representatives to obtain and enforce for its or their own benefit proper patent protection for said inventions or improvements in any and all countries.

AND we hereby authorize and request the Commissioner of Patents and Trademarks of the United States and any official of any country or countries foreign to the United States whose duty it is to issue patents on applications as aforesaid, to issue to said assignee, as assignee of the entire right, title and interest, any

DOCKET NO.: ISPH-0519 PATENT

and all Letters Patent for said inventions or improvements, including any and all Letters Patent of the United States which may be issued and granted on or as a result of the application aforesaid, in accordance with the terms of this assignment.

IN WITNESS WHEREOF, we have hereunto set our hands and seals.

| DATED:_ | 211 | _, | 2001 |
|---------|-----|----|------|
| DATED:_ | 211 | _, | 2001 |

BRETT P. MONIA

State of California)) ss.
County of San Diego)

LANE B.D. SCHWARTZ
Commission # 1196197
Notary Public - Callfamia
San Diego County
My Comm. Bupires Sep 13, 2002

WITNESS my hand and official seal.

Signature of Notary

PATENT DOCKET NO.: ISPH-0519 DATED: 1/31/01, 2001 State of California)
County of San Diego) On this 6/6 day of anuary, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Lex M. Cowsert, personally known to me/preved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment. WITNESS my hand and official seal. LANE B.D. SCHWARTZ Commission # 1196197 Notary Public - California San Diego County My Comm. Expires Sep 13, 2002 Signature of Notary

State of California SS. County of San Diego

Susan Murray, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in her authorized capacity, and that by her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



PATENT

DOCKET NO.: ISPH-0519

| DATED: <u>Jan 31</u> , 2001 | Modeline M. Butle |
|-----------------------------|----------------------------|
| State of California) | ss. |
| County of San Diego) | |
| On this 3184 day | of muary, 2001, before me, |

On this 3 day of Mullipped, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Madeline M. Butler, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in her authorized capacity, and that by her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

LANE B.D. SCHWARTZ
Commission # 1196197
Notary Public - California
San Diego County
My Comm. Expires Sep 13, 2002

WITNESS my hand and official seal.

Signature of Notary

 $DATED: 1/30 \qquad , 2001$

NICHOLAS M. DEAN

State of California

ss.

County of San Diego

On this day of <u>lanuary</u>, 2001, before me, the undersigned, a Notary Public for the state, personally appeared <u>Nicholas M. Dean</u>, personally known to me/proved to me on the <u>basis of satisfactory evidence</u> to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in her authorized capacity, and that by her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

ionature

LANE B.D. SCHWARTZ
Commission # 1196197
Notary Public - California
San Diego County
My Comm. Expres Sep 13, 2002

WITNESS my hand and official seal.

Table A

| N I Oin CO | Ciling Date | Inventor(s) | Examiner | Art | Title |
|---|--------------------------------------|--------------------|------------------|---------|---|
| Patent No. | Issue Date | | | | |
| 09/577,902 6,284,538 | May 24, 2000 September 4, 2001 | B. Monia et al. | M. Schmidt | 1635 | ANTISENSE INHIBITION OF PTEN EXPRESSION |
| 1SIS0004-102 09/048,810 6,238,921 ISIS0052-101 | March 26, 1998 May 29, 2001 | L. Miraglia et al. | M. Shibuya | 1635 | ANTISENSE OLIGONUCLEOTIDE MODULATION OF HUMAN MDM2 EXPRESSION |
| 09/280,805 6,184,212 | March 26, 1999 February 6, 2001 | L. Miraglia et al. | J. Epps | 1635 | ANTISENSE MODULATION OF HUMAN MDM2 EXPRESSION |
| 09/731,457 ISIS0053-100 | December 6, 2000 | I. Popoff et al. | J. Schultz | 1635 | ANTISENSE MODULATON OF DAMAGE SPECIFIC DNA BINDING PROTEIN 1, P127 EXPRESSION |
| 09/659,860 ISIS0054-100 | September 11, 2000 | H. Zhang et al. | J. Schultz | 1635 | ANTISENSE MODULATION OF CASPASE 7 EXPRESSION |
| 10/007,078 ISIS0055-100 | November 8, 2001 | D. Ward et al. | J. Schultz | 1635 | ANTISENSE MODULATION OF EIF2C1 EXPRESSION |
| 09/953,611 ISIS0056-100 | September 13, 2001 | D. Ward et al. | To Be Determined | 1635 | ANTISENSE MODULATION OF PROTEIN KINASE R EXPRESSION |
| 09/715,983 ISIS0057-100 | November 20, 2000 | B. Monia et al. | J. Zara | 1635 | ANTISENSE MODULATION OF PI3K P85 EXPRESSION |
| 09/344,521 6,100,090 | June 25, 1999 August 8, 2000 | B. Monia et al. | J. Zara | 1635 | ANTISENSE INHIBITION OF PI3K P85 EXPRESSION |
| 09/954,679 ISIS0058-100 | September 12, 2001 | D. Ward et al. | K. Lacourciere | 1635 | ANTISENSE MODULATION OF RIBONUCLEASE L EXPRESSION |
| 09/484,617 6,303,374 ISIS0059-100 | January 18, 2000 October 16, 2001 | H. Zhang et al. | S. McGarry | 1635 | ANTISENSE MODULATION OF CASPASE 3 EXPRESSION |
| | | | | | |

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| ON TOTAL | Filing Date | Inventor(s) | Examiner | Art | Title |
|---|---|------------------|------------------|------|---|
| Patent No. | Issue Date | | | Unit | |
| 09/679,298 6,566,131 | October 4, 2000 May 20, 2003 | L. Cowsert | M. Schmidt | 1635 | ANTISENSE MODULATION OF SMAD6 EXPRESSION |
| 09/679,299 6,566,135 | October 4, 2000 May 20, 2003 | A. Watt | J. Zara | 1635 | ANTISENSE MODULATION OF CASPASE 6 EXPRESSION |
| 09/853,768 6,444,466 | May 10, 2001 September 3, 2002 | D. Ward et al. | J. LeGuyader | 1635 | ANTISENSE MODULATION OF HELICASE- MOI EXPRESSION |
| 10/001,863 ISIS0063-100 | November 19, 2001 | J. Karras et al. | To Be Determined | 1645 | ANTISENSE MODULATION OF TOLL-LIKE RECEPTOR 4 EXPRESSION |
| 09/865,993 ISIS0064-100 | May 25, 2001 | B. Monia et al. | J. Zara | 1635 | ANTISENSE MODULATION OF DUAL SPECIFIC PHOSPHATASE 5 EXPRESSION |
| 09/667,018 ISIS0065-100 | September 20, 2000 | H. Zhang et al. | J. Schultz | 1635 | ANTISENSE MODULATION OF CASPASE 2 EXPRESSION |
| 10/271,887 ISIS0066-100 | October 15, 2002 | H. Zhang et al. | To Be Determined | 1635 | ANTISENSE MODULATION OF CASPASE 9 EXPRESSION |
| 09/659,845 6,492,170 | September 11, 2000 December 10, 2002 | A. Watt | A. Wang | 1639 | ANTISENSE MODULATION OF CASPASE 9 EXPRESSION |
| 10/309,362 ISIS0067-100 | December 3, 2002 | D. Ward et al. | To Be Determined | 1635 | ANTISENSE MODULATION OF RECQL5 EXPRESSION |
| 10/238,443 ISIS0067-101 | September 9, 2002 | D. Ward et al. | To Be Determined | 1635 | ANTISENSE MODULATION OF RECQL5 EXPRESSION |
| 09/798,185 ISIS0067-102 | March 1, 2001 | D. Ward et al. | K. Lacourciere | 1635 | ANTISENSE MODULATION OF RECOL5 EXPRESSION |
| 09/798,096 6,399,378 ISIS0068-100 | March 1, 2001 June 4, 2002 | D. Ward et al. | S. McGarry | 1635 | ANTISENSE MODULATION OF RECOLS EXPRESSION |

| Serial No. | Filing Date | Inventor(s) | Examiner | | Title |
|---|---------------------------------------|---------------------|------------------|------|--|
| Patent No. Docket No. | Issue Date | | | | |
| 09/792,594 6,436,706 | February 23, 2001 August 20, 2002 | D. Ward et al. | K. Lacourciere | 1635 | ANTISENSE MODULATION OF RECQL4 EXPRESSION |
| 09/793,807 ISIS0070-100 | February 23, 2001 | D. Ward et al. | J. Zara | 1635 | ANTISENSE MODULATION OF RECQL EXPRESSION |
| 09/358,381 6,020,199 | July 21, 1999 February 1, 2000 | B. Monia et al. | M. Schmidt | 1635 | ANTISENSE MODULATION OF PTEN EXPRESSION |
| 10/006,430 ISIS0072-100 | December 10, 2001 | M. Graham et al. | S. McGarry | 1635 | ANTISENSE MODULATION OF CD81 EXPRESSION |
| 10/175,492 ISIS0073-100 | June 17, 2002 | K. Dobie et al. | To Be Determined | 1645 | ANTISENSE MODULATION OF PAZ/PIWI DOMAIN CONTAINING PROTEIN EXPRESSION |
| 10/199,221 ISIS0074-100 | July 18, 2002 | B. Monia et al. | J. Epps | 1635 | ANTISENSE MODULATION OF DUAL SPECIFIC PHOSPHATASE 6 EXPRESSION |
| 09/487,444 6,159,697 | January 19, 2000 December 12, 2000 | B. Monia et al. | A. Wang | 1635 | ANTISENSE MODULATION OF SMAD7 EXPRESSION |
| 10/181,603 ISIS0075-101 | July 17, 2002 | B. Monia et al. | To Be Determined | 1651 | ANTISENSE MODULATION OF SMAD7 EXPRESSION |
| 09/732,199 6,379,960 ISIS0076-100 | December 6, 2000 April 30, 2002 | I. Popoff et al. | M. Schmidt | 1635 | ANTISENSE MODULATION OF DAMAGE- SPECIFIC DNA BINDING PROTEIN 2, p48 EXPRESSION |
| 09/920,668 6,482,644 ISIS0077-100 | August 1, 2001 November 19, 2002 | L. Cowsert | M. Schmidt | 1635 | ANTISENSE MODULATION OF DUAL SPECIFIC PHOSPHATASE 8 EXPRESSION |
| 09/922,146 6,566,133 ISIS0078-100 | August 1, 2001 May 20, 2003 | L. Cowsert | T. Gibbs | 1635 | ANTISENSE MODULATION OF DUAL SPECIFIC PHOSPHATASE 9 EXPRESSION |

| Serial No. Patent No. | Filing Date Issue Date | Inventor(s) | Examiner | Art Unit | Title | |
|--------------------------|---------------------------|----------------------------|------------------|-------------|--|---|
| Docket No. | | | | | O LOVEOVO LO MOLEVILLO LO LO CITATIONE DE LO COMPANIONE D | Г |
| 09/487,445 | January 19, 2000 | H. Zhang et al. M. Shibuya | M. Shibuya | 1635 | 1635 ANTISENSE MODULATION OF CASPASE & | |
| 6,258,600 | July 10, 2001 | | | | EXTRIBUTION | |
| ISIS0079-100 | | | | | | Т |
| 10/181,177 | July 12, 2002 | H. Zhang et al. | To Be Determined | 1632 | Zhang et al. To Be Determined 1632 ANTISENSE MODULATION OF CASPASE 8 | |
| ISIS0079-101 | | | | | EXPRESSION | |
| | | | | | | |